Applicants thank the Examiner for the courteous and helpful telephonic interview with the undersigned on June 27, 1996, at which time the above amendments and the rejections were discussed.

The claims were rejected for obviousness-type double patenting; for indefiniteness under 35 USC §112, ¶2; and for lack of patentable utility under 35 USC §101. These rejections are discussed below.

Obviousness-type Double Patenting

The rejection of the claims for obviousness-type double patenting over co-owned U.S. Patent No. 5,485,827 is overcome by the enclosed terminal disclaimer in compliance with 37 CFR §1.321. Applicants request that the rejection therefore be withdrawn.

35 USC §112, ¶2

The Examiner objected to use of terms such as "said mammal" and "said human" in the claims. These terms have been replaced with corresponding terms which the Examiner indicated would be acceptable, including "a mammal", "the mammal", "such a mammal", "a human", and the like. In addition, the phrasing "causing said mammal to inhale" in some of the claims has been replaced with "providing to a mammal for inhalation" or similar phrasing, as suggested by the Examiner. Withdrawal of the rejection under 35 USC §112, ¶2, is therefore requested.

35 USC §101

The Examiner rejected all of the pending claims for lack of patentable utility under 35 USC §101 "because of a lack of any recited means for preventing a patient from inhaling a toxic oxidized product of nitric oxide, namely nitrogen dioxide." As pointed out in the June 27, 1996, interview, and as acknowledged by the Examiner in that interview, this reasoning does not support a proper rejection under §101.

First, both the Commissioner of Patents and Trademarks and the Federal Circuit have explicitly stated that the safety of a pharmaceutical is a matter of concern solely for the Food and Drug Administration, not the Patent and Trademark Office (Manual of Patent Examining Procedure, §2107, page 2100-15, citing *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995)).[1]

Second, there is no question that Applicants have provided ample information about how to practice the invention safely. The specification describes the dangers of allowing the patient to inhale NO_2 (see, e.g., page 8, lines 30-31; page 6, lines 5-9; and page 22, lines 7-21); how NO_2 formation can be minimized (page 22, lines 7-11, and page 29, lines 12-14 and 18-20); and how to remove NO_2 from the NO-containing gas prior to inhalation (page 23, lines 19-21, and page 46, lines 3-5). Thus, the specification clearly enables one to practice the invention

[1] Nor would it be proper to reject the claims on similar grounds under 35 USC §112, §1. As stated in MPEP §2107(d), page 2100-15, a rejection under §112, ¶1 for lack of utility should not be imposed if a rejection under §101 is not proper.

safely, so that even if safety were an appropriate concern of the Patent and Trademark Office, the requirement would be met.

Third, the Office Action implies that the details of how to practice the invention safely must form part of the claims themselves. This view is unwarranted, and contrary to accepted law. U.S. patent law does not require that a claim include every step that must be followed or element that must be built in to ensure the safe practice of the invention. To do so would be ludicrous. Imagine if every method of treatment or therapeutic composition claim had to specify that equipment and drugs must be sterilized, that toxic overdoses must be avoided, and that patients must be screened for allergies to the drug prior to treatment. As an illustrative example in another field, consider a hypothetical claim drawn to an electric motor. A source of electricity, and presumably an electric cord connecting the motor to that source, would be essential for practicing the invention. However, neither §101 or §112, ¶1, would require including in the claim a limitation specifying that an electric cord be attached to the motor. Similarly, it is unnecessary to add to the present claims a limitation regarding how to minimize NO_2.

Fourth, Applicants point out that many of the claims do in fact explicitly address the NO_2 issue. Claims 77, 84, 93, 98, 107, 112, 115-119, 123, 126-129, and 132 specify either that the claimed apparatus include an NO_2 scavenger, or that the claimed method include an NO_2 scavenging (i.e., removal) step prior to inhalation, which is one way to minimize the NO_2 content of the inhaled gas. Claims 78, 85, 94, 99, 106, 110-114, 117, 122, 124-

126, 129, 131, and 134 require that the claimed device include an NO_2 analyzer or that the claimed method include an NO_2 monitoring step. Claims 83-86 specify that the claimed apparatus provide for a residence half time of NO in the gas reservoir of 15 seconds or less, which is one way to minimize the NO_2 content of the inhaled gas. Claims 104, 106-109, 120, and 122-123 specify that the NO_2 concentration in the gas mixture is less than 12 ppm; while claims 105, 111, 116, 121, 125, and 128 narrow that even further to less than 1 ppm NO_2. Thus, all of these claims do specifically address the NO_2 issue.

As indicated in the Examiner's Interview Summary Record mailed June 28, 1996, the Examiner now acknowledges that the rejection of the claims under 35 USC §101 for lack of safety was improper. Applicants submit that there is no other basis under 35 USC §101 or any other section of the statute for rejecting the claims for failure to recite a means for preventing a patient from inhaling NO_2.

It is noted that some but not all of the references listed on the Information Disclosure Statement form 1449 submitted March 9, 1995, were initialed by the Examiner. On the assumption that the Examiner was unable to find in the file for the parent case, USSN 07/767,234 (since issued as U.S. Patent No. 5,485,827), those references which he did not initial in the present case, Applicants submit herewith new copies of those references and request that the initialling of the form 1449 be completed. The re-submitted references are as follows:

AR Great Britain Patent No. 2178958 (2/87)

BF Kacmarek et al., Nitric Oxide as a Bronchodilator in Methacholine Induced Bronchospasm in Mild Asthmatics, 1993 ALA/ATS International Conference, May 16-19, 1993, San Francisco, CA #21556 (Abstract).

BG Messent et al., The Pulmonary Physician and Critical Care, Thorax 47:651-656, 1992.

BH Swami et al., the Pulmonary Physician and Critical Care, Thorax 47:555-562, 1992.

BI Frostell et al., Inhaled Nitric Oxide: A Selective Pulmonary Vasodilator Reversing Hypoxic Pulmonary Vasoconstriction, Circulation 83:2038-2047, 1991.

CA Tan et al., Cigarette Smoke Activates Guanylate Cyclase and Increases Guanosine 3′,5′-Monophosphate in Tissues, Science 198:934-936, 1977.

CD Moncada et al., Nitric Oxide: Physiology, Pathophysiology, and Pharmacology, Pharmacl. Reviews 91:109-141, 1991.

CE Kalant et al., Drugs and the Respiratory System, Chapter 39 362-397, 1989.

EC Ignarro, Biological Actions and Properties of Endothelium-Derived Nitric Oxide Formed and Released From Artery and Vein, Dept. Pharmlgy. 65:23-278, 1989.

FF Agabwal et al., Nature 205:915-916, 1965.

FL Oxytocin. Prostaglandins. Ergot Alkaloids. Tocolytic Agents., Chapter 39, pp. 942-945.

FM Resnick et al., Evaluation and Medical Management of Urinary Incontinence, Anesthesia, Seventh Edition, pp. 3-6, 1992.

FN Zapol et al., Regional Blood Flow During Simulated Diving in the Conscious Weddell Seal, J. Appl. Physiol. 47:968-973, 1979.

FP Jansen et al., The Relaxant Properties in Guinea Pig Airways of S-Nitrosothiols, J. Pharmacology and Experimental Therapeutics 261:154-160, 1992.

Applicants submit that all of the claims are now in condition for allowance, which action is requested. Filed herewith is a Petition for Automatic Extension with the required fee. In the unlikely event that the Petition and/or fee is separated from this Amendment or is insufficient, Applicants hereby petition for a one-month extension of time to respond to the Office Action mailed March 28, 1996, or any other required relief, and authorize the Commissioner to charge any required fees, or make any credits, to Deposit Account No. 06-1050.

Respectfully submitted,

Date: July 24, 1996

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